taken up by sympathetic neurons and cause the release of norepinephrine in supranormal amounts in nerve endings. This can lead to a severe adrenergic response, one of the most predominant being severe hypertension.[5] A third mechanism of interaction involves drugs that inhibit the reuptake of serotonin such as tricyclic antidepressants, serotonin reuptake inhibitors, meperidine hydrochloride, and dextromethorphan. The MAOI interaction with these drugs has been called "the serotonin syndrome" and manifests as restlessness, tremor, and monoclonus as a prelude to seizures and coma. The syndrome is thought to be caused by the combination of decreased serotonin degradation and the inhibition of reuptake.[6]

In cases of the overdose of MAOIs, symptoms include hypertension, tachycardia, flushing, tachypnea, pulmonary edema, hyperpyrexia, agitation, drowsiness, headache, seizures, and coma.[7] Of note is that profound hypotension, bradycardia, cardiovascular collapse, and asystolic arrest may follow the overdose of MAOIs alone.[8] If the treatment of hypotension is refractory to fluid replacement or other nonpharmacologic means, direct-acting sympathomimetics such as norepinephrine or dopamine may be used cautiously. This is because they are metabolized primarily by catechol *O*-methyltransferase and do not require the release of intracellular amines.[9]

The evaluation of a case of MAOI overdose should include a history of additional drug use such as sympathomimetic agents. It is important to recognize, however, that tranylcypromine and selegiline hydrochloride are metabolized to amphetamine-like structures and can be reported as such on toxicologic screens.[10] Our patient's positive toxicology screen for amphetamines was available within the first few hours, but given the confounding tranylcypromine metabolite, this information was of minimal usefulness.

This patient had numerous side effects that have been documented with MAOI overdose: hyperthermia that required the administration of acetaminophen and a cooling blanket, agitation that required large doses of lorazepam, and then seizures that required paralysis and intubation. Severe hypertension did not develop (for which nifedipine might have been used), nor did hypotension, bradycardia, cardiovascular collapse, or cardiac arrest. There was no evidence of the use of a serotonin reuptake inhibitor. Her toxicologic screen was positive for benzodiazepines—the patient was taking clonazepam—and amphetamines. Although the clonazepam may have played a role in the patient's respiratory depression,[11] the large quantities of midazolam and diazepam required for sedation were probably more substantial. The patient had taken an unknown over-the-counter cold medication that could have been the cause of the amphetamines in the toxicology screen. As stated earlier, tranylcypromine is metabolized to amphetamine-like structures, which could also account for these positive findings.

The treatment of patients with severe personality disorders is difficult and often fraught with risks, including overdose. Efforts are being made to produce more specific MAOIs, targeting enzyme subsets located primarily in the CNS.[12] Although it is hoped that such medications will provide patients the antidepressant effects of MAOIs without the grave risks of interactions, current information remains mixed.[13] With these new medications, the use of MAOIs may show a resurgence. Until then, the danger of interactions and overdose will continue to overshadow the use of these agents.

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Eosinophilic Tuberculous Pleural Effusion

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PLEURAL FLUID EOSINOPHILIA is defined as greater than 10% eosinophils in the pleural leukocyte differential count, and as many as 8% of cases of exudative pleural effusions are eosinophilic.[1] The most common conditions associated with eosinophilic pleural effusions are previous thoracen-

(Bassiri AG, Morris W, Kirsch CM. Eosinophilic tuberculous pleural effusion. West J Med 1997 Apr; 166:277–279)

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tesis, air or blood in the pleural cavity, asbestosis, collagen-vascular disease, drug-induced pleuritis, paragonimiasis, and malignancy.[2] In a recent authoritative book on pleural disease, the author stated that "if eosinophils are found in the pleural fluid in significant numbers (>10%), one can exclude the diagnosis of tuberculous pleuritis unless the patient has a pneumothorax or has had a previous thoracentesis."[3(pp156-157)] The increasing incidence of tuberculosis (TB), however, may be associated with more cases of eosinophilic tuberculous pleurisy than previously recognized.[4] We describe the case of a patient with eosinophilic tuberculous pleurisy and review the pertinent literature.

Report of a Case

The patient, a 23-year-old Filipino man, was referred to the Santa Clara Valley Medical Center (San Jose, California) with one month of dry cough, night sweats, a 2.3-kg (5-lb) weight loss, and a right pleural effusion (Figure 1). A tuberculin skin test was positive four years before this presentation, but the patient was never treated with isoniazid. His mother (2 years before) and brother (4 years before) had been treated for active tuberculosis. He did not smoke, use illicit drugs, or consume alcohol. He had no other medical problems and was taking no regular medications.

On physical examination the patient was thin and had normal vital signs, including a temperature of 37°C. There were dullness and decreased breath sounds throughout the lower half of the posterior right side of the chest. No other abnormalities were elicited. Laboratory investigations revealed a peripheral blood leukocyte count of 6.7 × 10^9 per liter (6,700 per mm^3) with eosinophilia (neutrophils 0.61 [61%], lymphocytes 0.19 [19%], monocytes 0.11 [11%], and eosinophils 0.08 [8%]). Sputum staining was negative for acid-fast bacilli. A diagnostic thoracentesis revealed straw-colored fluid with a leukocyte count of 3.9 × 10^9 per liter (3,900 per mm^3), with 0.61 lymphocytes, 0.36 eosinophils, 0.02 monocytes, and 0.01 neutrophils; an erythrocyte count of 13.1 × 10^9 per liter (13,100 per mm^3); total protein value, 63 grams per liter (6.3 grams per dl) (plasma protein, 81 grams per liter); lactate dehydrogenase level, 399 U per liter (serum lactate dehydrogenase, 180 U per liter); and glucose level, 3.9 mmol per liter (70 mg per dl) (serum glucose, 5 mmol per liter). A Gram's stain, routine culture, acid-fast bacilli and fungal stains and culture, and cytologic examination of the pleural fluid were all negative for pathogens. An Abrams needle biopsy of the right pleura showed granulomas with Langhans' giant cells but no acid-fast bacilli or fungus on special stains. Serologic tests for *Coccidioides immitis* and three stool specimens for ova and parasites were negative.

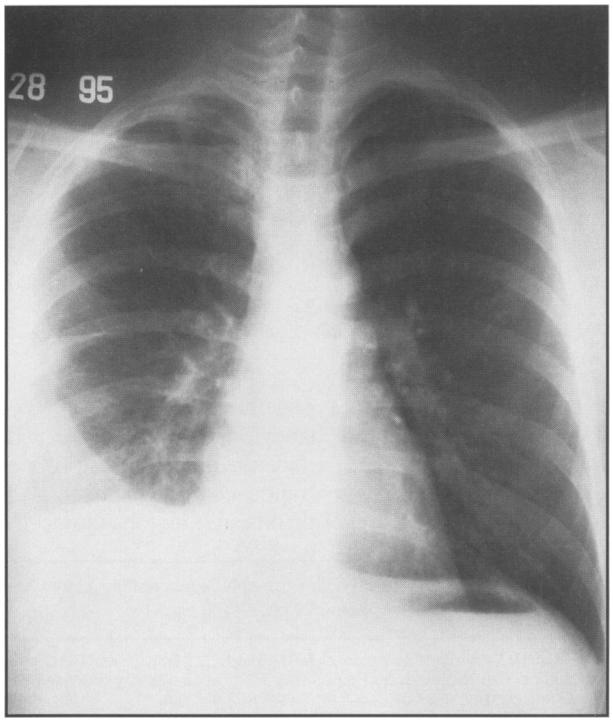

Figure 1.—The chest roentgenogram at presentation reveals a moderate-sized right pleural effusion.

Treatment was initiated with oral isoniazid, rifampin, pyrazinamide, ethambutol hydrochloride, and pyridoxine hydrochloride. A month after his presentation, two sputum cultures grew *Mycobacterium tuberculosis* resistant to isoniazid, and this drug and pyridoxine were discontinued. Pleural tissue cultures did not grow *M tuberculosis*. After six months of triple-drug therapy, the patient was asymptomatic, his sputum cultures were negative for *M tuberculosis*, the serum eosinophil fraction had decreased to 0.04 (4%) (leukocyte count, 4.2 × 10^9 per liter), and his effusion had resolved.

Discussion

Tuberculous pleurisy can be a difficult diagnosis to establish. At our institution, pleural fluid smears are rarely positive, and pleural fluid cultures recover organisms in about 30% of cases.[5] Pleural biopsy will yield positive results in about 70% to 81% of cases, usually in the form of granulomas.[5,6] Pleural tissue cultures grow tubercle bacilli in about 65% of cases.[6] In our study, 15% of patients with tuberculous pleurisy had normal pleural fluid and tissue studies, and the diagnosis of TB was established by sputum cultures.[5]

Pleural fluid eosinophilia is usually considered strong evidence against TB. In fact, according to one authority, the finding of pleural fluid eosinophilia excludes the diagnosis of tuberculous pleurisy.[3] Eosinophilic effusions have been described in 8 of 141 patients with presumed tuberculous pleurisy. The diagnosis of tuberculous pleurisy was based on a pleural biopsy specimen showing epithelioid granulomas; only 55% of patients had tuberculous bacilli recovered from sputum, pleural fluid, or gastric aspirates.[7] In a review of 78 cases of eosinophilic pleural effusions from the same (Scandinavian) center, 9 patients were found on pleural biopsy to have epithelioid granulomas and 5 patients had nonspecific biopsy findings but concomitant pulmonary TB.[8] Neither of these reviews indicated whether previous thoracenteses had been done on individual patients. Furthermore, it is possible that some of the pleural epithelioid granulomas identified were not due to TB. In

fact, other studies have failed to report similar incidence rates. In the largest series of 500 cases of tuberculous pleural effusion from three North Carolina sanatoriums, only one patient had pleural eosinophilia.[9] In a review of these studies and nine others (all of which failed to elicit any case of tuberculous eosinophilic effusions), it was concluded that the finding of an eosinophilic pleural effusion decreases the likelihood of TB by tenfold.[1]

The spontaneous resolution of tuberculous pleural effusion is well known.[3] Untreated, spontaneously resolved tuberculous pleural effusions, however, are likely (60% to 65%) to subsequently reappear as active tuberculous pneumonia.[3] Therefore, the spontaneous resolution of an eosinophilic pleural effusion in a patient at risk for TB should not be construed as evidence against this diagnosis.

Tuberculous eosinophilia has been reported in other body fluids. Eosinophilia was reported in the bronchoalveolar lavage fluid of three patients with tuberculous pneumonia and resolved in the two patients who completed a full course of treatment.[10] One of these patients had a blood eosinophil fraction of 0.74 (74%) that decreased to 0.03 (3%) with antituberculous treatment. Of the 14 patients with tuberculous pleural eosinophilic effusions described by Kokkola and Valta, 4 had 0.07 (7%) or higher blood eosinophilia.[8] Similarly, our patient had an initial peripheral eosinophilia of 0.08 (8%) that decreased to 0.04 (4%) after treatment.

This case shows that an eosinophilic pleural effusion may be caused by TB. The availability of curative therapy and the increasing incidence of TB obligate consideration of this diagnosis despite the finding of an eosinophilic pleural effusion.

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